Hemolytic Anemia Following Valvuloplastic Surgery for Congenital Mitral Regurgitation : Report of Two Cases

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Hemolytic Anemia Following Valvuloplastic Surgery for Congenital Mitral Regurgitation : Report of Two Cases

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Abstract

Two patients who developed hemolytic anemia following valvuloplastic surgery for congenital mitral regurgitation were reported. Recurrent mitral regurgitation due to break down of the annuloplasty and non-endothelialized large Teflon felts found at the posterior annulus were responsible for the hemolysis of the first, 3-year-old boy and the Lillehei-Kaster tilting disc valve was inserted in place. Delayed endothelialization of the Teflon felts used for reinforcement of sutures and protection of the mitral annulus was presumed to be the origin of hemolysis in the second, 8-year-old girl. Her hemolytic anemia disappeared spontaneously.

It is now widely accepted that a slight degree of hemolytic anemia develops after prosthetic ball valve replacement on account of red cell damage by direct contact between the rigid valve housing and the rigid ball[1]. It occurs more commonly in the aortic position than in the mitral. Although employment of a prosthetic tilting disc valve seems to reduce the incidence of hemolytic anemia as compared to a ball valve prosthesis[8], paravalvular leakage, delayed endothelialization of the

Key words : Hemolytic anemia, Congenital mitral regurgitation, Valvuloplastic surgery, Recurrent regurgitation, Non-endothelialized Teflon felt.

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valve housing, fibrin strands, turbulance and hemodynamic alterations[2] increase the grade of hemolytic anemia so severe as to necessitate re-replacement of the defective valve prosthesis.

Artificial materials other than valve prosthesis also can occasionally develop hemolytic anemia of cardiac origin. Among these, repair of an ostium primum defect with a Teflon patch is a common sort of operation that induces hemolytic anemia[4),5),6),9)], whereas reports of hemolytic anemia following valvuloplastic surgery for mitral regurgitation are fairly rare[2),3),10),11)].

The authors present two cases who developed hemolytic anemia following valvuloplastic surgery for congenital mitral regurgitation — in this term used here, mitral regurgitation associated with an endocardial cushion defect and corrected transposition of the great arteries is not included —, one of whom was treated with mitral valve replacement with a Lillehei-Kaster tilting disc valve and the other had spontaneous subsidence of her anemia.

Patients

Case 1. K. S., a 3-year-old Japanese boy was born on January 21, 1973 following a full-term and normal delivery. Birth weight was 3,260 gram. At the age of 3 months this boy was found to have cardiac enlargement when he consulted his family doctor on account of poor sucking and fever. Cardiac catheterization performed at the age of 5 months revealed coarctation of the aorta and mitral insufficiency.

On July 9, 1973, resection of the coarctation of the aorta with end to end anastomosis of the descending aorta was performed. His postoperative course was uneventful. The patient had been doing well until facial edema and liver enlargement developed and digitalis with diuretics was started at the age of 2 years and 11 months. On August 8, 1976, at the age of 3 years and 7 months, the second cardiac catheterization was performed and the results showed mitral and tricuspid insufficiency (Fig. 1).

Open heart surgery was performed on November 8, 1976 at the Kyoto University Hospital. Opening of the left atrium revealed a hypoplastic commissural leaflet, a cleft in the posterior part of the anterior leaflet and a dilated mitral annulus. The papillary muscle was single and was classified as a sort of parachute mitral valve. Regurgitant flow of blood seemed to come from mainly the posterior commissural region. A cleft of the anterior leaflet was sutured with six interrupted stitches. Mitral annuloplasty was done at the anterior and posterior commissural region with interrupted U-stitches using Teflon felts for protection of the mitral annulus. The diameter of the mitral orifice was decreased from 28 to 12 mm. The right atrium was opened and a tricuspid annuloplasty was performed so as to approximate the posterior leaflet region with U-stitches.

On the tenth postoperative day, a systolic blowing murmur was heard over the

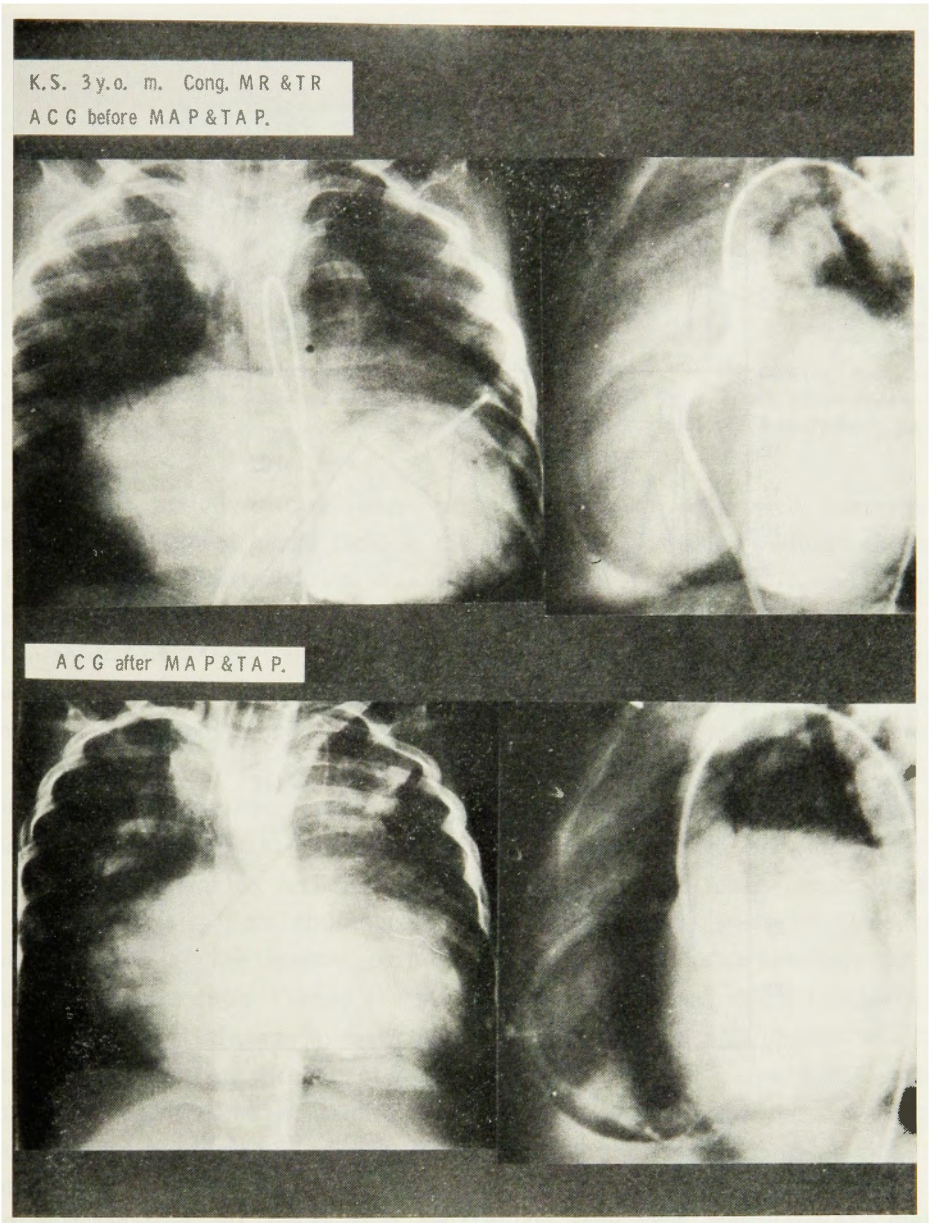

Fig. 1

apex and axillary regions. The heart on chest roentgenogram did not show any decrease in size. At the same time slight jaundice was noticed in the skin and conjunctivae. Anemia was detected with red blood cells of $303\times10^4/cm^3$, hemoglobin 8.8 g/dl and a hematocrit of 29.0 per cent. The subsequent course of peripheral blood is shown in Fig. 2. The reticulocyte count increased and ranged from 2.2 to 34.4 per cent. The thrombocyte count decreased to the lowest value of $8.2\times10^4/cm^3$.

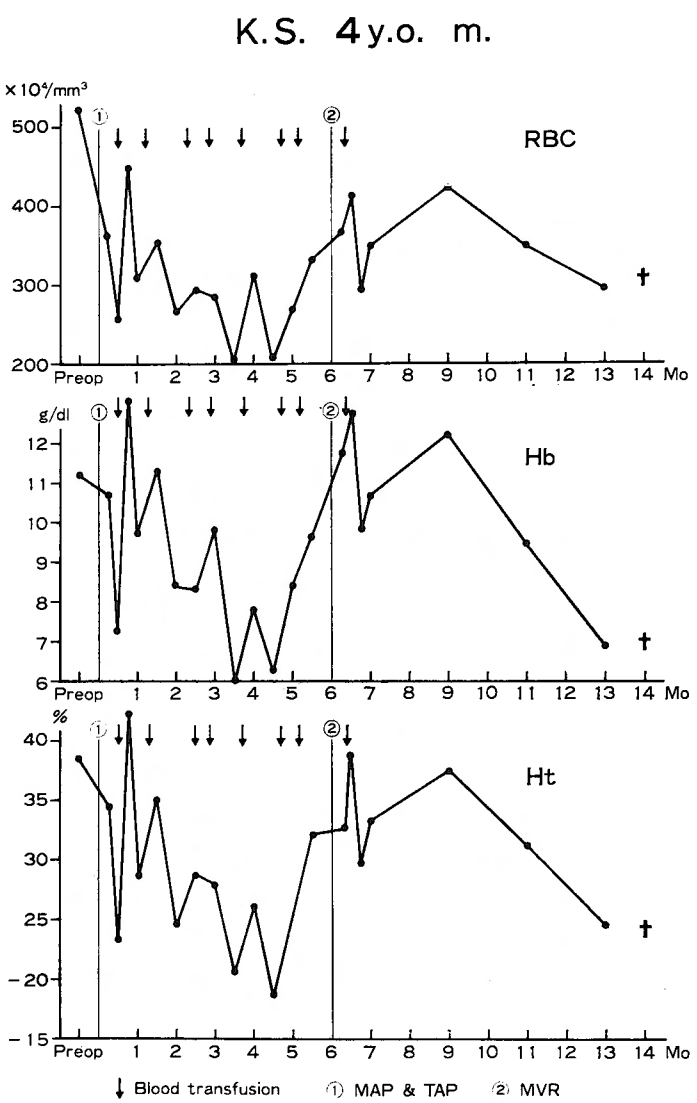

Fig. 2 Case 1. Serial changes of RBC, Hb and Ht.

Lactate dehydrogenase was over 600 mU/ml throughout the postoperative period. The total bilirubin increased to a level of 6.0 mg/dl. Blood films showed fragmented red cells, poikilocytosis and anisocytosis (Fig. 3). The apparent half-life of the red cells labelled with ^{51}Cr was shortened to 5.2 days. Haptoglobin was 2.4 mg/dl and serum hemoglobin was 64 mg/dl. Unsaturated iron binding capacity was low with 114 microgram Fe/dl, whereas serum iron was within normal. Fibrin degradation products were less than 10 r/ml and fibrinogen was 242 mg/dl. The direct and indirect Coomb's tests were negative.

Fresh washed red cells were given seven times —200 to 800 ml per time— over

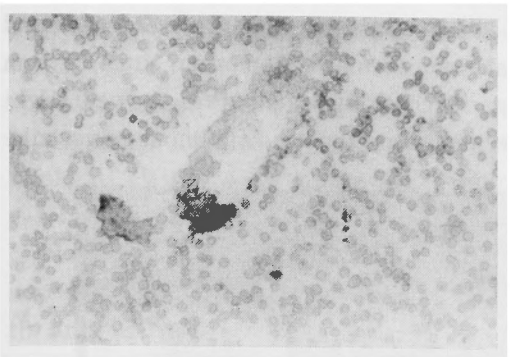

Fig. 3 Case 1. Blood film shows fragmented red cells, poikilocytosis and anisocytosis.

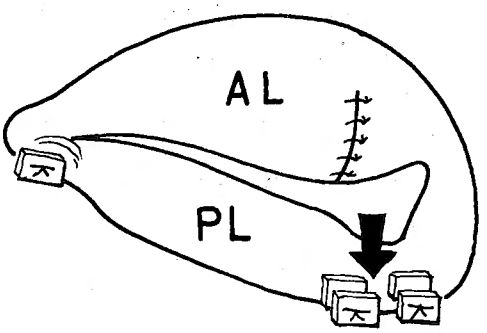

Fig. 4 Case 1. Sketch of the reexplored mitral valve. Black arrow shows the direction of the regurgitant jet of blood.

a five months period without improvement. Signs of congestive heart failure persisted with a dilated heart, fluid in the thorax cavity, liver swelling and ascites. The third cardiac catheterization was performed on April 14, 1977 and recurrent mitral regurgitation of grade IV/IV was confirmed (Fig. 1).

The second open heart surgery was performed on May 9, 1977. Re-exploration of the mitral valve revealed recurrence of regurgitation due to a break down of the stitches put at the posterior commissure. The Teflon felts used for reinforcement of the stitches and protection of the mitral annulus were found at the posterior annular region of the posterior commissure. They were not covered with endothelium and seemed to be too large. A regurgitant jet of blood impinged upon the bare and large Teflon felts making turbulance. Sutures of the cleft in the anterior leaflet were intact (Fig. 4). Two annuloplastic procedures, at the posterior commissural region first and at the central part of the posterior annulus subsequently, were attempted unsuccessfully. Finally the mitral valve was excised and a Lillehei-Kaster tilting disc valve (14M) was inserted in place. The tricuspid annuloplasty was intact on inspection. However, the patient had a stormy postoperative course with cerebral complications and died of pneumonia and general weakness eight months after the second open heart surgery. On autopsy progressive sclerosing cortical atrophy was found.

Case 2. M. I., an 8-year-old Japanese girl, was born on July 1, 1968 following a full term and normal delivery. Her birth weight was 3600 grams. At the age of 1 year and 5 months, she was noted to have a heart murmur. She was admitted to the Kyoto University Hospital for investigation of her heart on May 1977. Physical examination revealed a well developed, moderate sized girl with normal blood pressure and pulse. There was a thrill and thrust over the apical region. A grade 4 harsh blowing systolic murmur was heard over the apex and transmitted to the axilla. There was neither liver swelling nor pretibial edema. The lungs were clear

on auscultation. Red blood cells were $486\times10^4/cm^3$. Hemoglobin was 13.7 g/dl and hematocrit 40.2 per cent. Electrocardiogram showed normal axis, normal sinus rhythm and tendency to left ventricular hypertrophy. A chest roentgenogram showed slight enlargement of the left atrium and ventricle and almost normal pulmonary vascula-

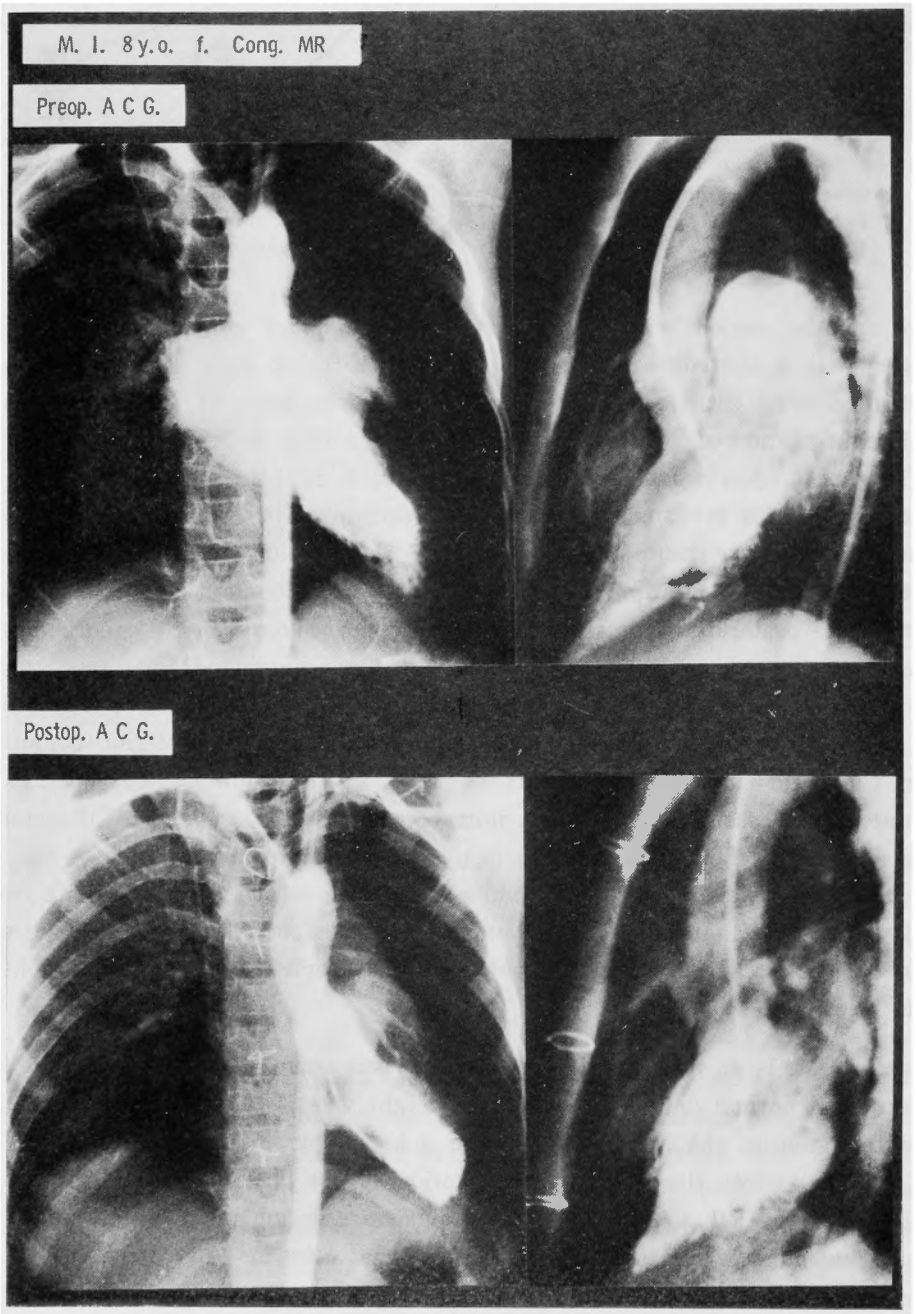

Fig. 5

ture. Echocardiography showed an increased left atrial dimension and an increased amplitude of the anterior mitral leaflet. Cardiac catheterization revealed normal pressure in the right side of the heart and the pulmonary capillary wedge pressure at the upper limit of normal. A left ventriculogram showed mitral regurgitation of grade III/IV and an enlarged left atrium (Fig. 5).

The patient underwent open heart surgery on August 24, 1977 at the Mitsubishi Kyoto Hospital. The mitral valve was regurgitant. There was a cleft in the mid-portion of the posterior leaflet. There was slight hypertrophy in the valve at the tip area of the cleft presumably due to the regurgitant jet of blood. The chordae tendineae around the cleft were normally thin and pliable. The cleft was sutured with interrupted stitches and annuloplasty was performed using Teflon felts for reinforcement of the sutures at the posterior commissural region. The diameter of

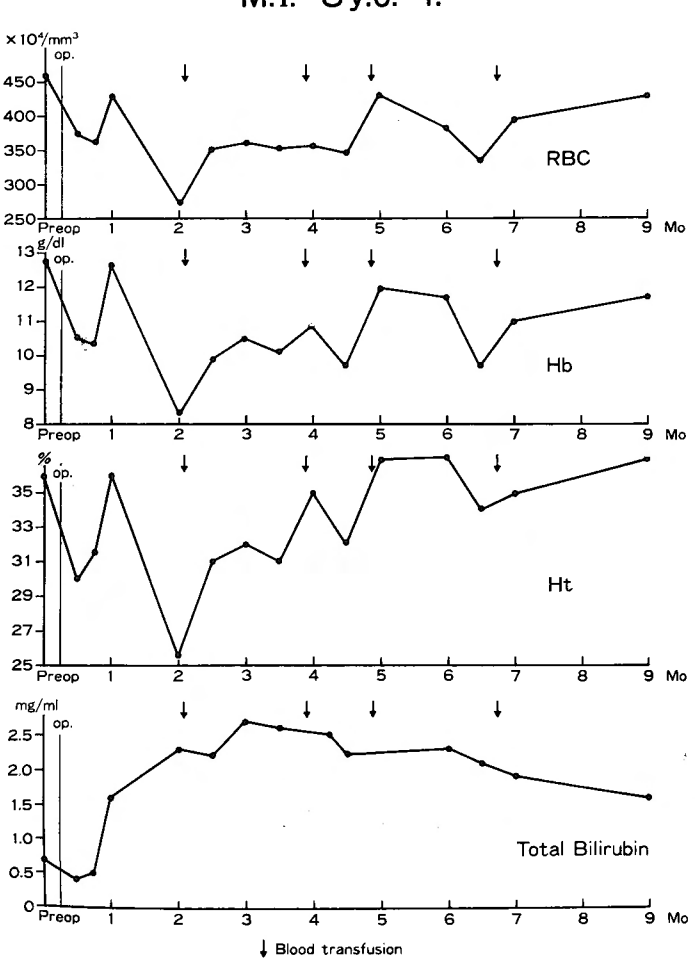

Fig. 6 Case 2. Serial changes of RBC, Hb, Ht and total bilirubin.

the mitral valve orifice was shortened from 35 to 24 mm. There was a small amount of residual regurgitation on examination during surgery. Her immediate postoperative course was uneventful. However, anemia developed two months postoperatively with a hemoglobin of 8.3 g/dl and hematocrit of 25.5 per cent. There was an increase of total bilirubin to a maximum of 2.7 mg/dl and the indirect bilirubin was 1.9 mg/dl. Subsequent changes of her red blood cells, hemoglobin, hematocrit and total bilirubin values are shown in Fig. 6. The reticulocyte count increased to 9.0 per cent. A postoperative left ventriculography confirmed the residual mitral regurgitation of grade I/IV (Fig. 5). A decision was made not to reexplore her mitral valve and to follow-up with blood transfusion. Two units of blood were given four times over a six months period. Thereafter the anemia subsided spontaneously and the patient has done well for over three months wothout receiving blood.

Discussion

Development of anemia, existence of fragmented cells, poikilocytosis and anisocytosis in the blood films, shortening of red cell survival time, increased total bilirubin with jaundice, increased lactate dehydrogenase, reticulocytosis, decreased haptoglobin and increased serum hemoglobin supported the diagnosis of intravascular hemolytic anemia following mitral valvuloplastic surgery. Although laboratory data were scanty in the second patient, the clinical course strongly suggested transient hemolytic anemia presumably due to delayed endothelialization of the Teflon felts in the heart.

Existence of residual mitral regurgitation itself is not necessarily responsible for the development of hemolytic anemia following mitral valvuloplastic surgery. In the twenty-nine patients who have undergone this kind of operation by our hands, four of them got complete subsidence of mitral regurgitation, while the rest have evidence of mitral regurgitation of slight to moderate degree without development of hemolytic anemia except in the two cases reported here.

The reexplored mitral valve of the first case showed recurrence of severe mitral regurgitation from the posterior commissural region. This was due to break down of the stitches placed at this part. The Teflon felts used for reinforcement of suture and protection of the mitral annulus were exposed to the regurgitant jet of blood at the posterior annulus and were not covered with endothelium. Moreover these Teflon felts seemed to be too large. It was presumed that the bare and large Teflon surface was greatly responsible for the damage of red cells due to contact with the turbulance of the regurgitant jet of blood.

An eight-year-old boy, one of two patients reported by Yenko et al[10]. developed hemolytic anemia following mitral annuloplasty for congenital mitral insufficiency. In the first operation a large dilated mitral annulus was repaired by suturing bolsters of woven Teflon to both anterior and posterior commissures. Mitral

regurgitation recurred with the occurrence of hemolytic anemia. At the second operation, it was noted that the Teflon bolster, placed at the postorior commissure, had partially torn loose from its silk suture. It was projecting, as a small kernel, into the mitral orifice. This Teflon presumably would have been in contact with the flow of blood. The Starr-Edwards valve was inserted in place. But the patient could not tolerate the operation. Ziperovich and Paley reported a 23-year-old woman who developed hemolytic anemia on account of severe mitral insufficiency after open mitral commissurotomy with valvular repair[11]. At a second operation, the previous repair of the tear in the anterior leaflet was found to have broken down resulting in massive regurgitation. The Starr-Edwards prosthetic valve was inserted in place and hemolysis ceased almost completely. Moisey and colleagues reported a 4-year-old boy who had undergone repair of a cleft in the anterior leaflet with polyester sutures[2]. Hemolytic anemia developed one month after operation about the same time when a moderately loud systolic murmur was heard at the apex. Reexploration of the mitral valve revealed several sutures adjacent to the lateral commissure, one of which was relatively loose. It seemed likely that the red cell damage occured at this site. Mitral valve replacement was carried out with an OM composite-seat Starr-Edwards prosthetic valve followed by cessation of the hemolytic anemia. O'Regan and Newman presented a 9-year-old girl who had developed hemolytic anemia after mitral annuloplasty for severe mitral incompetence of cardiac origin[3]. She had a second mitral annuloplasty with resolution of hemolysis. However, no anatomical finding presumed to be the cause of disability was described in their report. Sigler et al. reported three cases of atrioventricular defect who developed hemolytic anemia following closure of the defect and suture of the cleft[6]. The septal repair had pulled away from where it had been sutured to the mitral valve, thus producing a new cleft or tear in the mitral valve. The Teflon felt was well endothelialized and the congenital defects which had been sutured in the first operation was intact. Correction of these new clefts resulted in abrupt cessation of hemolysis in the first patient, but another patient could not tolerate the second operation. Sayed et al. reported a 25-year-old man with an ostium primum defect who had reexploration of his mitral valve on account of postoperative hemolytic anemia[5]. It was found that a regurgitant jet of blood through a cleft in the mitral valve had been impinging on a bare Teflon surface. This bare area had formed the base of a little cul-de-sac. The adjacent edge of endocardium were sutured over the bare area to provide a complete and satisfactory cover. This procedure resulted in complete cessation of hemolytic anemia. Verdon et al. presented two cases in which the bare Teflon patch was likely to be responsible for postoperative hemolytic anemia after repair of an ostium primum defect[9].

Hemolytic anemia of the second patient reported here subsided by giving several units of whole blood. This patient has residual mitral regurgitation of slight degree.

Suture of the cleft and posterior annuloplasty with Teflon felts were the procedures performed. It would seem likely that the delayed covering of the Teflon felts with endothelium was the cause of the hemolytic anemia and hemolysis subsided presumably with complete endothelialization of the Teflon felts.

A similar kind of speculation is reported by Singh and others[7]. They presented hemolysis following correction of double-outlet right ventricle which disappeared spontaneously after six postoperative weeks. They presumed that spontaneous subsidence of the hemolysis was due to endothelialization of the Dacron patch used for reconstruction of the outflow tract in the right ventricle.

Recurrent mitral regurgitation due to inadequate repair is most likely to be a predisposing factor and other situations, such as existence of prosthetic material, incomplete covering of foreign substances with endocardium, contact of prosthetic material with regurgitant jet of blood and turbulance, contribute greatly to the development of hemolytic anemia following valvuloplastic surgery. Every effort should be employed to reduce regurgitation as perfectly as possible at the time of surgery. If a slight amount of regurgitation is obliged to be kept in situ, direction of the regurgitant jet of blood is checked to see whether or not it impinges upon the Teflon felt. Furthermore, Teflon felts used for reinforcement of the sutures and also for protection of the mitral annulus should be small enough necessary for bites.

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和文抄録

先天性僧帽弁閉鎖不全症に対する弁形成術後に発生した溶血性貧血の2例

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先天性僧帽弁閉鎖不全症に対する弁形成術後に溶血性貧血を来した2例を経験したので報告した．第1例は4才男子．生後7ヶ月の時大動脈縮窄症に対する手術を受けている．3才10ヶ月の時先天性僧帽弁閉鎖不全症に対して弁形成及び弁輪縫縮術，合併する三尖弁閉鎖不全症に対して三尖弁輪縫縮術を施行した．術後10日目頃より僧帽弁逆流音を聴取するようになると同時に貧血と黄疸を発症した．赤血球数，Hb，Ht の経過は図2に示す．網状赤血球 2.2−34.4%，赤血球半減期5.2日，ハプトグロビン 2.4mg/dl，血漿ヘモグロビン 64mg/dl，LDH 600mU/ml 以上．末梢血塗沫標本に赤血球断片，大小不同症，異形赤血球症を認めた。洗滌新鮮赤血球を1回200万至 800ml，5ヶ月の間に7回投与したが改善せず，術後6ヶ月，再開心術を行った．僧帽弁は初回手術で行った後交連部の縫縮が離脱しており，この部分より逆流が再発．逆流の Jet は弁輪縫縮の補強に用いた Teflon felt を直撃していたと判断出来た．この Teflon felt は全く器質化していなかったうえに必要よりもやや大きめであった．僧帽弁を切除し Lillehei-Kaster ディスク弁で置換した．しかし術後患者は脳障害を併発し，stormy な経過を辿ったのち再手術後8ヶ月目に死亡した．第2例は8才女子。逆流度Ⅲ度の先天性僧帽弁閉鎖不全症に対して弁形成及び弁輪縫縮術を施行した．術後2ヶ月頃より貧血，網状赤血球増多を認め，血清総ビリルビン値も高値を示すようになった．術後の左室造影で逆流度Ⅰ度の遺残逆流を認めたが再手術の必要はないと判断し，1回 400mlの輸血を6ヶ月の間に4回行って貧血は回復した．以後順調に経過している．

第1例にあっては逆流の再発と心内膜で被覆されない大きな Teflon felt の存在が溶血の発生に関与したと考えており，第2例についても弁輪縫縮に用いた Teflon felt の心内膜による被覆遅延が原因であったと推測している．